## Remarks

Applicant has carefully reviewed this Application in light of the Office Action sent 26 February 2009. To expedite issuance of a patent from this Application, Applicant has made clarifying amendments to Claims 1, 9, 11, 19, 21, 29 and 31. Applicant has added new Claims 32-43. Applicant respectfully requests the Examiner to reconsider and allow all pending claims.

## Interview Summary

Applicant thanks the Examiner for the 9 April 2009 telephone interview. The Examiner entered an Interview Summary 23 April 2009 summarizing the telephone interview. The Interview Summary entered by the Examiner is consistent with the substance of the telephone interview. As the Examiner stated, Applicant discussed a proposed amendment to Claim 1 adding a limitation that a local binding environment of the atom pair is considered. At the conclusion of the telephone interview, Applicant agreed to file this Response.

## Claims 21 and 29-30 Recite Patentable Subject Matter

The Examiner rejects Claims 21 and 29-30 under 35 U.S.C. 101 as being directed to nonstatutory subject matter. Although Applicant does not necessarily agree with the Examiner, to expedite issuance of a patent from this Application, Applicant has amended independent Claim 21 to recite *software encoded in one or more computer-readable storage media*, which the Specification of this Application, as originally filed, provides at least sufficient support for. As an example, the Specification includes the following description:

FIGURE 1 illustrates an example system 10 for calculating a PMF score of a protein-ligand complex. System 10 includes a computer system 12 and a PMF-scoring module 14. In particular embodiments, a module may include software, hardware, or both. Computer system 12 may enable a user to provide input to and receive output from PMF-scoring module 14. Computer system 12 may include one or more modules for generating one or more graphical user interfaces (GUIs) for providing input to and receiving output from PMF-scoring module 14. PMF-scoring module 14 may calculate one or more PMF scores of

one or more protein-ligand complexes specified by a user and return the calculated PMF scores to the user. A PMF score of a protein-ligand complex may indicate the binding affinity between the protein and the ligand in the protein-ligand complex, and the binding affinity between the protein and the ligand in the protein-ligand complex may indicate the ability of the ligand to inhibit or otherwise modify the function of the protein. PMF-scoring module 14 includes a repulsion-term module 16 that may calculate one or more repulsion terms, as described below. PMF-scoring module 14 may use PMF-scoring data 18 to calculate a PMF score of a protein-ligand complex. PMF-scoring data 18 data that PMF-scoring module 14 may use to calculate a PMF score of a protein-ligand complex. In particular embodiments, PMF-scoring data 18 includes empirically derived parameters (such as minimum binding-energy distance and well-depth values) that may be used to calculated a PMF score of a protein-ligand complex, as described below. Although components of system 10 are described and illustrated as being separate from each other, the present invention also contemplates any suitable components of system 10 being combined with any other suitable components in any suitable manner. As an example and not by way of limitation, in particular embodiments, PMF-scoring module 14 is executed at computer system 12. As another example, in particular embodiments, PMF-scoring data 18 is stored at computer system 12.

(Specification, Page 5, Lines 2-28). For the convenience of the Examiner, Applicant provides the following reproduction of FIGURE 1:



FIG. 1
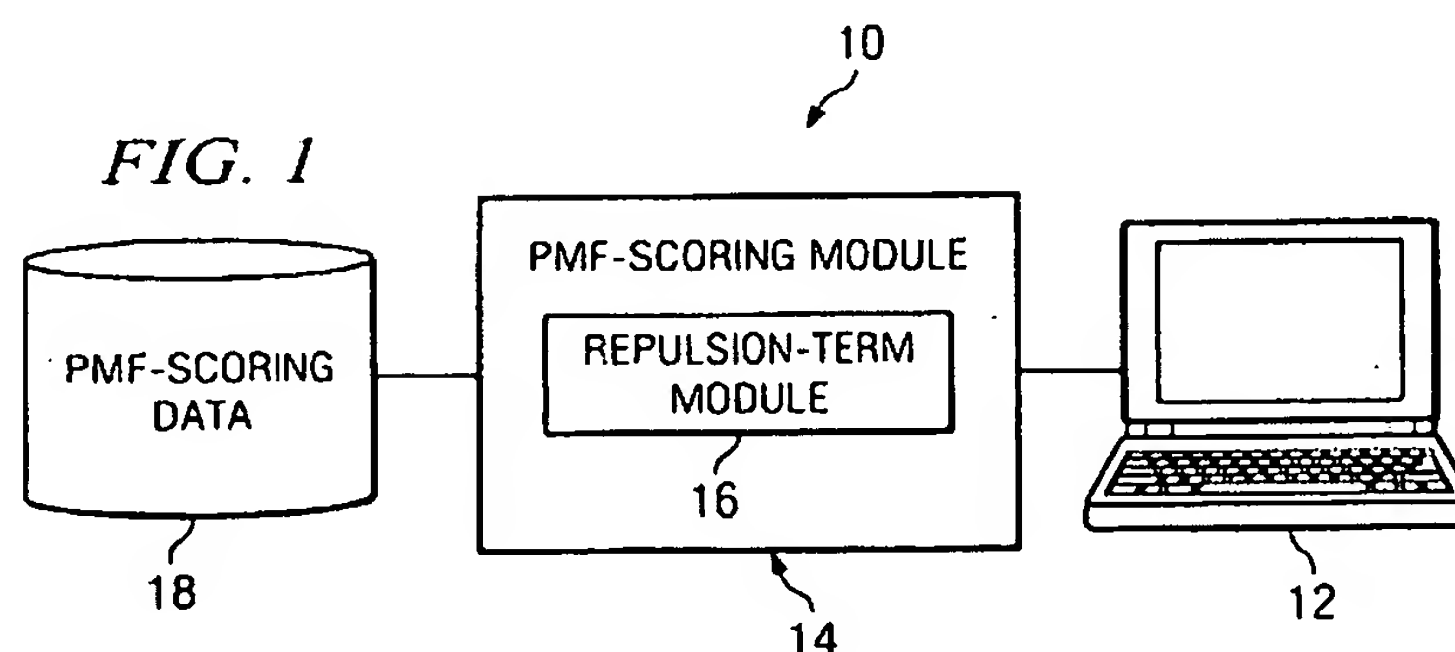
Applicant respectfully submits that at least these portions of this Application, as originally filed, provide support for *computer-readable storage media*, as independent Claim 21 recites. The Examiner states, "The specification at the time of filing did not describe any form of

computer readable media." For at least the reasons discussed above, Applicants respectfully disagree with the Examiner. Dependent Claims 29-30 depend on independent Claim 21.

Moreover, even though sufficient description of physical computer readable media exists, to expedite issuance of a patent from this Application, Applicant hereby states that the claims do not read on embodiments that are not physical computer-readable media.

### Independent Claim 11 Recites Patentable Subject Matter

The Examiner rejects Claim 11 under 35 U.S.C. 101 as being directed to nonstatutory subject matter. Although Applicant does not necessarily agree with the Examiner, to expedite issuance of a patent from this Application, Applicant has made clarifying amendments to independent Claim 11. Applicant respectfully requests the Examiner to reconsider and allow independent Claim 11 and all its dependent claims.

### Claims 21 and 29-30 Comply with 35 U.S.C. § 112, Para. 1

The Examiner rejects Claims 21-22, 25, 27, and 29-30 under 35 U.S.C. § 112, para. 1, as failing to comply with the written description requirement. Applicant notes that Applicants previously canceled Claims 22, 25, and 27. Although Applicant does not necessarily agree with the Examiner, to expedite issuance of a patent from this Application, Applicant has amended independent Claim 21 to recite *software encoded in one or more computer-readable storage media*, which, as Applicant discusses above, the Specification of this Application, as originally filed, provides support for.

Applicant respectfully requests the Examiner to reconsider and allow independent Claim 21 and all its dependent claims.

## Independent Claims 1, 11, 21, and 31 are Allowable Over the Proposed *Muegge I-Mitchell-Muegge II* Combination

The Examiner rejects independent Claims 1, 11, 21, and 31 under 35 U.S.C. § 103(a) as being unpatentable over Ingo Muegge et al., *Evaluation of PMF Scoring in Docking Weak Ligands to the FK506 Binding Protein*, J. MED. CHEM., Vol. 42, Pages 2498-503 (1999) ("*Muegge I*") in view of John B.O. Mitchell et al., *BLEEP—Potential of Mean Force Describing Protein-Ligand Interactions: I. Generating Potential*, J. COMP. CHEM., Vol. 20, No. 11, Pages 1165-76 (1999) ("*Mitchell*") and in further view of Ingo Muegge, *The Effect of Small Changes in Protein Structure on Predicted Binding Modes of Known Inhibitors of Influenza Virus Neuraminidase: PMF-Scoring in Dock4*, MED. CHEM. RES. Vol. 9, pages 490-500 (1999) ("*Muegge II*"). Although Applicant does not necessarily agree with the Examiner, to expedite issuance of a patent from this Application, Applicant has made clarifying amendments to independent Claims 1, 11, 21, and 31.

Applicant respectfully submits that the proposed *Muegge I-Mitchell-Muegge II* combination fails to disclose, teach, or suggest all the limitations of independent Claim 1. As an example, the proposed *Muegge I-Mitchell-Muegge II* combination fails to disclose, teach, or suggest *determining an atom-pair type of a protein-ligand atom pair in a protein-ligand complex, the protein-ligand atom pair comprising a protein atom and a ligand atom, the protein atom comprising a first element and having a first local bonding environment that comprises the ligand atom, the ligand atom comprising a second element and having a second local bonding environment that comprises the protein atom, the atom-pair type being defined by the first and second elements and the combination of local bonding environments*, as independent Claim 1 recites. As another example, the proposed *Muegge I-Mitchell-Muegge II* combination fails to disclose, teach, or suggest *the first and second local bonding environments each comprising a polar aliphatic bonding environment, a nonpolar aliphatic bonding environment, a polar aromatic bonding environment, a nonpolar aromatic bonding environment, a hydrogen bond donor bonding environment, or a hydrogen bond acceptor*

*bonding environment*, as independent Claim 1 recites. As yet another example, the proposed *Muegge I-Mitchell-Muegge II* combination fails to disclose, teach, or suggest *determining a minimum binding-energy distance value for the protein-ligand atom pair based on the atom-pair type, the minimum binding-energy distance value representing a distance corresponding to a minimum binding-energy for the atom-pair type*, as independent Claim 1 recites. As yet another example, the proposed *Muegge I-Mitchell-Muegge II* combination fails to disclose, teach, or suggest *determining a well-depth value for the protein-ligand atom pair based on the atom-pair type, the well-depth value representing an amount of binding interaction for the atom-pair type*, as independent Claim 1 recites.

Independent Claims 11, 21, and 31, as amended, recite similar limitations to independent Claim 1.

Applicant respectfully requests the Examiner to reconsider and allow independent Claims 1, 11, 21, and 31 and all their dependent claims.

### Independent Claims 1, 11, 21, and 31 are Allowable Over the *Muegge I-Mitchell-Muegge II-Morris* Combination

The Examiner also rejects independent Claims 1, 11, and 21 under 35 U.S.C. § 103(a) as being unpatentable over *Muegge I*, in view of *Mitchell*, in view of *Muegge II*, and further in view of Garrett M. Morris et al., *Automated Docking Using a Lamarckian Genetic Algorithm and an Empirical Binding Free Energy Function*, J. COMP. CHEM. Vol. 19, No. 14, Pages 1639-1662 (1998) ("*Morris*"). Although Applicant does not necessarily agree with the Examiner, to expedite issuance of a patent from this Application, Applicant has made clarifying amendments to independent Claims 1, 11, 21, and 31.

Applicant respectfully submits that the proposed *Muegge I-Mitchell-Muegge II* combination fails to disclose, teach, or suggest all the limitations of independent Claim 1. As an

example, the proposed *Muegge I-Mitchell-Muegge II* combination fails to disclose, teach, or suggest ***determining an atom-pair type of a protein-ligand atom pair in a protein-ligand complex, the protein-ligand atom pair comprising a protein atom and a ligand atom, the protein atom comprising a first element and having a first local bonding environment that comprises the ligand atom, the ligand atom comprising a second element and having a second local bonding environment that comprises the protein atom, the atom-pair type being defined by the first and second elements and the combination of local bonding environments***, as independent Claim 1 recites. As another example, the proposed *Muegge I-Mitchell-Muegge II* combination fails to disclose, teach, or suggest ***the first and second local bonding environments each comprising a polar aliphatic bonding environment, a nonpolar aliphatic bonding environment, a polar aromatic bonding environment, a nonpolar aromatic bonding environment, a hydrogen bond donor bonding environment, or a hydrogen bond acceptor bonding environment***, as independent Claim 1 recites. As yet another example, the proposed *Muegge I-Mitchell-Muegge II* combination fails to disclose, teach, or suggest ***determining a minimum binding-energy distance value for the protein-ligand atom pair based on the atom-pair type, the minimum binding-energy distance value representing a distance corresponding to a minimum binding-energy for the atom-pair type***, as independent Claim 1 recites. As yet another example, the proposed *Muegge I-Mitchell-Muegge II* combination fails to disclose, teach, or suggest ***determining a well-depth value for the protein-ligand atom pair based on the atom-pair type, the well-depth value representing an amount of binding interaction for the atom-pair type***, as independent Claim 1 recites.

Independent Claims 11, 21, and 31, as amended, recite similar limitations to independent Claim 1.

Applicant respectfully requests the Examiner to reconsider and allow independent Claims 1, 11, 21, and 31 and all their dependent claims.
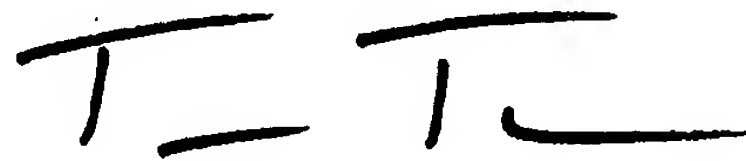
## Conclusion

For at least the foregoing reasons, Applicant respectfully requests the Examiner to reconsider and allow all pending claims.

If a telephone conference would advance prosecution of this Application, the Examiner may call Travis W. Thomas, Attorney for Applicant, at 650.739.7503.

The Commissioner may charge any fee due and credit any overpayment to Deposit Account No. 02-0384 of BAKER BOTTS L.L.P.

Respectfully submitted,

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